


BMJ Open All-cause excess mortality among end-stage renal disease (ESRD) patients during the COVID-19 pandemic in Thailand: a cross-sectional study from a national-level claims database

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ABSTRACT

Objectives COVID-19 infection increased nephrology-related risks and mortality rate among end-stage renal disease (ESRD) patients. The pandemic also disrupted essential healthcare services. We aim to explore all-cause excess mortality among ESRD patients who were members of the Universal Coverage Scheme (UCS), the largest public health insurance scheme in Thailand covering citizens who are not employed in the formal sector, including children and older persons.

Design A cross-sectional study.

Setting We retrieved the dataset from the UCS claims database—electronic health records used for processing healthcare expense claims from medical facilities of all UCS members. This database links mortality outcome to civil registration. We employed the WHO's excess mortality methodology using pre-pandemic data to estimate expected deaths during the pandemic period (March 2020 to August 2022).

Participants This study included ESRD patients from across Thailand, covered by the UCS.

Primary outcome measure Excess deaths are the difference between predicted and reported deaths.

Results Over a 30-month period of the pandemic, the total number of all-cause excess deaths among ESRD patients was 4966 (male 1284; female 3682). The excess death per 100 000 ESRD patients was 3601 (male 2012; female 4969). The relative excess death was 5.7% of expected deaths (95% CI 1.7%, 10.0%). The excess deaths were highly concentrated among patients aged 65 and older.

Conclusion ESRD patients are significantly more vulnerable to pandemic-related mortality than the general population. Health systems' capacity to contain the pandemic at varying virulence and maintain essential health services for ESRD patients might be related to the size of excess deaths at different periods. The observed excess deaths highlight the importance of established strategies to reduce all-cause mortality such as rapid vaccine rollout for ESRD patients and sustaining dialysis and other essential services for older patients and other high-risk groups.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study used a national-level claims database of the Universal Coverage Scheme, which covers 71% of Thai citizens; thus, ensuring representativeness of end-stage renal disease (ESRD) patients and minimising potential sampling bias.
- ⇒ The study used death statistics from Thailand's high-quality death registration, which has a coverage rate of 99.3% of total deaths. This high coverage enhances the accuracy of reported mortality outcomes.
- ⇒ The study followed the WHO's standard methodology for estimating excess mortality, providing a robust framework for analysing the impact of the COVID-19 pandemic on ESRD patients and facilitating comparison between studies.
- ⇒ Monthly incidence of newly diagnosed ESRD patients was estimated based on historical service utilisation profiles dating back to January 2016 only, which may introduce inaccuracies in the data.
- ⇒ Some ESRD patients may have been underdiagnosed during the pandemic, potentially affecting the accuracy of patient counts; particularly during waves 2 and 3 of the pandemic when healthcare systems were overwhelmed.

INTRODUCTION

The COVID-19 pandemic has profoundly impacted human lives, especially those in vulnerable situations. Travel restrictions have resulted in unemployment and economic disruption with an uneven recovery; a double shock as described by the World Bank.¹

In Thailand, the first confirmed case of COVID-19 was reported on 13 January 2020, marking the onset of a series of waves that swept the nation as well as policy responses.² There were four waves of the epidemic. The first wave began in March 2020, with a rapid increase in COVID-19 cases. This surge was



primarily caused by mass gatherings at Lumpini boxing stadium and entertainment venues in Bangkok. The second wave, from December 2020 to March 2021, was characterised by an outbreak among undocumented migrant workers.³ During this wave, the predominant viral variant was clade GH.⁴ The third wave, April to December 2021, was associated with an outbreak linked to an entertainment venue in Bangkok. Compounded by the relaxation of restrictions during the Thai New Year holidays in April 2021, the disease rapidly spread nationwide, overwhelming healthcare services. Notably, this wave was caused by Alpha, Beta and Delta variants, all of which were classified by the WHO as Variants of Concern, with a high mortality rate.³ August 2021 marked Thailand's highest number of daily confirmed COVID-19 cases (23 418) and confirmed deaths (312).⁵ The fourth wave, spanning from late 2021 to the end of 2022, caused by the Omicron variant with lower severity,⁶ marked a significant improvement in mortality as Thailand achieved high COVID-19 vaccine coverage. The Ministry of Public Health prioritised several population groups including end-stage renal disease (ESRD) patients, with a higher risk of COVID-19 mortality for receiving the COVID-19 vaccination; as evidence suggested that vaccination reduced mortality.⁷

ESRD is the final stage of chronic kidney disease (CKD), defined by a glomerular filtration rate of less than 15 mL/min. Patients with ESRD require regular renal replacement therapy (RRT) to continue survival. RRT includes haemodialysis (HD), peritoneal dialysis (PD) and kidney transplantation.⁸ In Thailand, the prevalence of people receiving RRT in 2020 was 170 774.⁹ A study conducted on Thai ESRD patients found that the 1-year, 2-year and 3-year patient survival rates were 84.4%, 77.3% and 72.7%, respectively.¹⁰

A study in 2021 showed that the COVID-19 pandemic had a negative impact on catheter insertion rates, outpatient follow-up visits and home visits for ESRD patients.¹¹ Another study confirmed that patients on HD and PD with SARS-CoV-2 infection had significantly increased mortality and complications such as coronary artery disease and congestive heart failure.¹² ESRD patients had an increased risk of mortality from COVID-19 as they have lower immune functions and multiple comorbidities. COVID-19 patients with ESRD had significantly higher odds of all-cause 1-year mortality compared with COVID-19 patients without ESRD.¹³ Although ESRD as a comorbidity that increased disease severity and mortality from COVID-19 has been well documented,¹⁴ the overall impacts on mortality due to the pandemic that is, disruptions of other essential services remains unknown.

Several studies have explored excess mortality resulting from COVID-19, including a study in Italy,¹⁵ and a systematic analysis covering multiple countries.¹⁶ Another study estimated that 14.83 million excess deaths occurred in the general population worldwide from 2020 through 2021, compared with 5.42 million COVID-19 reported deaths. The excess death per 100 000 population was 57.63 in 2020, which increased to 132.22 in 2021.¹⁷ An analysis in

the USA estimated a total of 6953–10 316 excess deaths in 798 611 ESRD patients which is equivalent to 870.6–1291.7 excess deaths per 100 000 ESRD patients.¹⁸ These studies shed light on the overall impact of COVID-19 on ESRD mortality. There remains a gap in the understanding of excess mortality rate and profiles among ESRD patients in Thailand, a middle-income country, in order to inform appropriate national policies.

In this study, we aim to estimate all-cause excess mortality among Thai ESRD patients during the COVID-19 pandemic. We focused on ESRD patients covered by the Universal Coverage Scheme (UCS) which was the largest public health insurance scheme in Thailand covering citizens who do not have other public health insurance schemes, that is, the informal sector, children and older persons. UCS covered 71% of all citizens.¹⁹ This subset represents approximately 40% of the total ESRD patients who were on RRT in 2020.⁹

METHODS

Data sources

We retrieved the dataset from the National Health Security Office (NHSO) which administers the UCS. The dataset included electronic health records of all outpatient and inpatient services of UCS members submitted for claims by health facilities. The mortality of any Thai citizen was captured by the Bureau of Registration Administration through death registration, as mandated by law, and linked daily with the UCS database by citizen ID. The dataset contained citizen ID, sex, age, hospital code, service date, principal diagnosis, secondary diagnoses, date and causes of death. NHSO encrypted citizen ID to protect personal data.

Study participants

Our study population was ESRD patients who were members of the UCS and used outpatient or inpatient services between January 2016 and August 2022. ESRD patients were identified based on the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision code: I185 as either their principal diagnosis or secondary diagnoses. We excluded a total of 2239 ESRD patients whose sex, age and death date were missing from our analysis (online supplemental figure 1).

Patient and public involvement

No patients involved.

Data management

We estimated monthly number of ESRD patients for the period between January 2016 and August 2022 using the following steps. First, we used the number of ESRD patients who were still alive at the end of 2015 as a baseline number. Second, for each month, we estimated incidence of ESRD cases by counting the patients who appeared in the service records for the first time since January 2016. Third, we counted the number of deaths

in each month. Finally, the number of ESRD population in month n is equal to the number of populations in the previous month ($n-1$) plus the difference between incident cases (new cases) and deaths in month n . Deaths related to COVID-19 were retrieved from cause of death information in the death registration system and were also counted monthly. All statistics were disaggregated by sex and the following age groups: 0–19 years, 20–44 years, 45–64 years, 65–74 years and ≥ 75 years.

We categorised the outbreak patterns into four distinct waves namely wave 1 (March–November 2020); wave 2 (December 2020–March 2021); wave 3 (April–December 2021); and wave 4 (January 2022–August 2022).

Statistical analysis

We followed the WHO’s manual for estimating excess mortality associated with COVID-19.²⁰ The WHO defines excess mortality as “the mortality above what would be expected based on the non-crisis mortality rate in the population of interest”.²¹ We modelled monthly all-cause mortality based on a negative binomial distribution to account for overdispersion of data using general additive models with covariates, namely the logarithm of monthly ESRD population, sex, age groups and a smooth function of time accounting for seasonal fluctuation with a penalised cyclic cubic regression spline (more details in online supplemental file box 1).

Excess mortality was estimated using three steps. First, we built the model to estimate the number of all-cause mortality using data from the pre-pandemic period. Second, we used the model to predict the number of expected deaths with a 95% CI for the no-outbreak scenario from March 2020 to August 2022. Third, we subtracted expected deaths during the outbreak period from the observed deaths to obtain excess deaths. We produced three figures (1) number of all-cause excess mortality, (2) excess deaths per 100 000 ESRD patients and (3) relative excess death as a per cent of expected

deaths, as described below where t refers to monthly observation.

$$\text{Excess deaths}_t = \text{observed deaths}_t - \text{expected deaths}_t$$

$$\text{Excess deaths per 100 000}_t = (\text{excess deaths}_t / \text{ESRD population}_t) \times 100\,000$$

$$\% \text{ relative excess deaths}_t = [(\text{observed deaths}_t - \text{expected deaths}_t) / \text{expected deaths}_t] \times 100$$

The model was fitted using *mgcv* package V.1.8-40 in R V.4.2.1.²²

RESULTS

Between January 2016 and August 2022, the UCS database recorded a total of 3 886 582 service records by 352 373 ESRD patients. After excluding 2239 patients with missing important data (accounting for 0.63%), there were 350 134 ESRD patients in our analysis cohort (see figure 1). The number of ESRD patients under the UCS ranged between 109 826 and 130 426 during 2016 and 2021. There were 134 520 ESRD patients at the end of August 2022. The median ages ranged between 65 and 66 years old and there were more females than males (females 52.8%–56.0%, males 44.0%–47.2%) throughout the observed years. Before the pandemic, over half the patients were aged 65 and above. However, once the pandemic began in 2020, the percentage of patients in this age group dropped below 50%. All-cause mortality counts substantially increased from 27 648 in 2016 to 40 510 in 2021. There were a total of 21 726 deaths among ESRD patients in 2022 (recorded until August). Mortality rate, as measured by the proportion of ESRD patients who died, increased from 25.2% in 2016 to 31.1% in 2021, and 16.2% in the 8 months of 2022. Females accounted for 54.1%–55.2% of total deaths in all observed years (see table 1).

Figure 1 compares monthly observed deaths (blue line) and expected deaths (solid red line with 95% CI in dashed red lines) over the coloured background indicating the

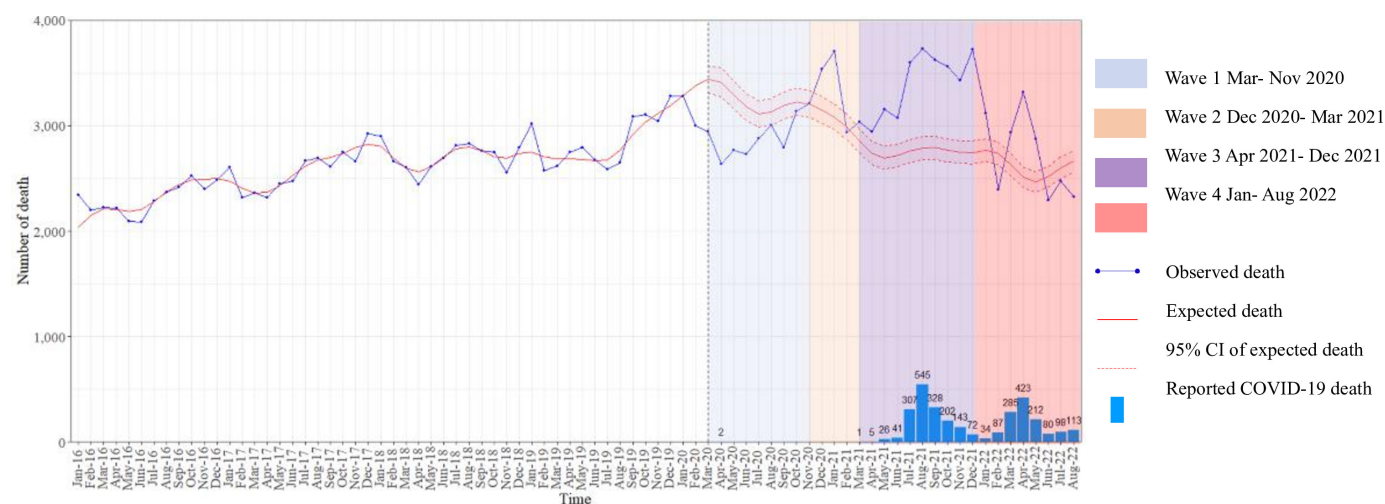


Figure 1 Monthly observed and expected all-cause mortality among end-stage renal disease patients between January 2016 and August 2022

Table 1 Characteristics and all-cause mortality of end-stage renal disease (ESRD) patients (January 2016 to August 2022)

	2016	2017	2018	2019	2020	2021	2022*
ESRD population, n	109 826	126 783	136 417	141 386	141 185	130 426	134 520
Median age, years	65 (56–74)	65 (57–74)	66 (57–74)	66 (57–74)	66 (57–74)	65 (56–73)	65 (56–72)
Age group, n (%)							
0–19	634 (0.6)	770 (0.6)	902 (0.7)	1081 (0.8)	1214 (0.9)	1362 (1.0)	1486 (1.1)
20–44	8091 (7.4)	9973 (7.9)	11 530 (8.5)	12 810 (9.1)	14 257 (10.1)	15 244 (11.7)	16 222 (12.1)
45–64	38 763 (35.3)	45 573 (35.9)	50 311 (36.9)	54 031 (38.2)	56 174 (39.8)	54 483 (41.8)	56 514 (42.0)
65–74	30 961 (28.2)	35 330 (27.9)	37 646 (27.6)	38 545 (27.3)	37 772 (26.8)	33 589 (25.8)	34 530 (25.7)
75 or more	31 377 (28.6)	35 137 (27.7)	36 028 (26.4)	34 919 (24.7)	31 768 (22.5)	25 748 (19.7)	25 768 (19.2)
Sex, n (%)							
Male	48 283 (44.0)	56 314 (44.4)	61 086 (44.8)	64 010 (45.3)	64 783 (45.9)	60 981 (46.8)	63 469 (47.2)
Female	61 543 (56.0)	70 469 (55.6)	75 331 (55.2)	77 376 (54.7)	76 402 (54.1)	69 445 (53.2)	71 051 (52.8)
Incident cases, n	57 561	47 798	42 053	39 147	35 721	29 751	25 820
Death, n	27 648	30 841	32 419	34 178	35 922	40 510	21 726
Mortality rate (% of ESRD population)	25.2%	24.3%	23.8%	24.2%	25.4%	31.1%	16.2%
Death by age group, n (%)							
0–19	82 (0.3)	92 (0.3)	74 (0.2)	90 (0.3)	80 (0.2)	77 (0.2)	49 (0.2)
20–44	1350 (4.9)	1441 (4.7)	1507 (4.6)	1626 (4.8)	1577 (4.4)	1949 (4.8)	1072 (4.9)
45–64	8775 (31.7)	9656 (31.3)	10 082 (31.1)	10 547 (30.9)	11 194 (31.2)	12 912 (31.9)	7139 (32.9)
65–74	7902 (28.6)	8698 (28.2)	9290 (28.7)	9749 (28.5)	10 378 (28.9)	11 837 (29.2)	6338 (29.2)
75 or more	9539 (34.5)	10 954 (35.5)	11 466 (35.4)	12 166 (35.6)	12 693 (35.3)	13 735 (33.9)	7128 (32.8)
Death by sex, n (%)							
Male	12 389 (44.8)	13 895 (45.1)	14 815 (45.7)	15 617 (45.7)	16 484 (45.9)	18 572 (45.8)	9890 (45.5)
Female	15 259 (55.2)	16 946 (54.9)	17 604 (54.3)	18 561 (54.3)	19 438 (54.1)	21 938 (54.2)	11 836 (54.5)

*Data up to 31 August 2022.

pre-pandemic period and the four waves during the pandemic. The red lines in the pandemic period go downward reflecting a reduced number of ESRD population. The graph presents the volume of positive and negative excess deaths during different waves, highlighting large numbers of excess deaths during the third wave caused by the Delta strain in the fourth quarter of 2021. The blue bar chart represents much lower numbers of monthly reported COVID-19-related deaths, though we observed a synchronous trend with all-cause death tolls of ESRD patients.

Table 2 shows monthly reported COVID-19 deaths among ESRD patients, observed all-cause deaths and estimated all-cause excess mortality in this group. Over the 30-month observation period, the total observed all-cause deaths were 91 879 while total expected deaths were 86 913. This resulted in total excess deaths of 4966. The excess deaths were 3600.9 per 100 000 ESRD patients, and the relative excess deaths were 5.7% of the expected number (95% CI 1.7%, 10.0%). The number of monthly

excess deaths was above zero in 17 out of 30 months. At the beginning of the pandemic, between March and October 2020, monthly excess deaths were negative, meaning there were fewer deaths than expected. The number of excess deaths turned positive between November 2020 and August 2022, except for the months of February 2021, February 2022 and June to August 2022. Consistently, relative excess death was negative in 2020 (–8.3%, 95% CI –11.8, –4.5), it rose to 20.3% of expected deaths (95% CI 15.7, 25.2) in 2021, and then reduced to 4.0% (95% CI 0.1, 8.2) in 2022. Though the excess deaths per 100 000 ESRD patients were mostly negative in 2020, it increased to between 127.3 and 750.6 deaths per 100 000 patients in 2021 (except for a negative value in February 2021). It is worth noting a significant reduction in the numbers of monthly ESRD population in 2021; from 140 785 in January to 130 426 in December. The excess deaths fluctuated in 2022.

Excess deaths were disaggregated by sex and age group. Out of the total positive excess deaths, 40% were males

Table 2 Monthly number of deaths caused by COVID-19, observed all-cause deaths and all-cause excess mortality among end-stage renal disease (ESRD) patients between March 2020 and August 2022

	ESRD patients (n)	Reported COVID-19 deaths (n)	Observed all-cause deaths (n)	Estimated all-cause mortality			Relative excess death, % of expected	
				Expected deaths (n)	Excess deaths (n)	Excess death per 100 000 (n)	%	95% CI
March 2020	141 301	0	2944	3441	-497	-351.7	-14.4	-10.8 to 18.1
April 2020	141 030	2	2635	3411	-776	-550.2	-22.7	-18.8 to 26.8
May 2020	140 909	0	2767	3294	-527	-374.0	-16.0	-12.0 to 20.0
June 2020	141 151	0	2733	3178	-445	-315.3	-14.0	-10.0 to 17.9
July 2020	141 169	0	2882	3111	-229	-162.2	-7.4	-3.3 to 11.4
August 2020	141 173	0	3006	3130	-124	-87.8	-4.0	-0.1 to 7.9
September 2020	141 336	0	2794	3189	-395	-279.5	-12.4	-8.3 to 16.4
October 2020	141 660	0	3134	3225	-91	-64.2	-2.8	1.1 to 6.8
November 2020	141 662	0	3211	3208	3	2.1	0.1	4.0 to 3.8
December 2020	141 185	0	3537	3147	390	276.2	12.4	16.4 to 8.4
March–December 2020	141 243	2	29643	32334	-2691	-1905.2	-8.3	-11.8 to 4.6
January 2021	140 785	0	3704	3082	622	441.8	20.2	24.0 to 16.3
February 2021	140 603	0	2937	2988	-51	-36.3	-1.7	2.3 to 5.7
March 2021	140 639	1	3035	2856	179	127.3	6.3	10.2 to 2.3
April 2021	139 842	5	2944	2740	204	145.9	7.4	11.4 to 3.5
May 2021	139 069	26	3154	2696	458	329.3	17.0	21.0 to 12.9
June 2021	138 396	41	3072	2719	353	255.1	13.0	16.9 to 9.1
July 2021	137 014	307	3600	2759	841	613.8	30.5	34.5 to 26.5
August 2021	135 601	545	3729	2789	940	693.2	33.7	37.6 to 29.8
September 2021	134 423	328	3622	2791	831	618.2	29.8	33.7 to 25.8
October 2021	133 230	202	3559	2767	792	594.5	28.6	32.6 to 24.7
November 2021	132 053	143	3432	2753	679	514.2	24.7	28.5 to 20.8
December 2021	130 426	72	3722	2743	979	750.6	35.7	39.7 to 31.7
January–December 2021	135 606	1670	40 510	33 683	6827	5034.4	20.3	15.7 to 25.2
January 2022	130 827	34	3116	2768	348	266.0	12.6	16.4 to 8.7
February 2022	131 597	87	2392	2736	-344	-261.4	-12.6	-8.7 to 16.5
March 2022	132 276	285	2934	2630	304	229.8	11.6	15.5 to 7.6
April 2022	132 105	423	3319	2511	808	611.6	32.2	36.0 to 28.3
May 2022	132 673	212	2875	2467	408	307.5	16.5	20.6 to 12.5
June 2022	133 637	80	2294	2517	-223	-166.9	-8.9	-5.0 to 12.7
July 2022	134 160	98	2472	2601	-129	-96.2	-5.0	-1.0 to 8.9
August 2022	134 520	113	2324	2666	-342	-254.2	-12.8	-8.9 to 16.7
January–August 2022	132 674	1332	21 726	20 896	830	625.7	4.0	0.1 to 8.2
March 2020–August 2022	137 911	3004	91 879	86 913	4966	3600.9	5.7	1.7 to 10.0

and 60% were females. The oldest age group (75 years and over) accounted for the largest proportion (59%), followed by the 65 to 74-year group (30%), and the 45 to 64-year group (11%). Those below 45 years had only

31 excess deaths (0%). Numbers are reported in online supplemental table 1.

We estimated the relative excess deaths as per cent of expected deaths, by sex and age group in figures 2 and 3,

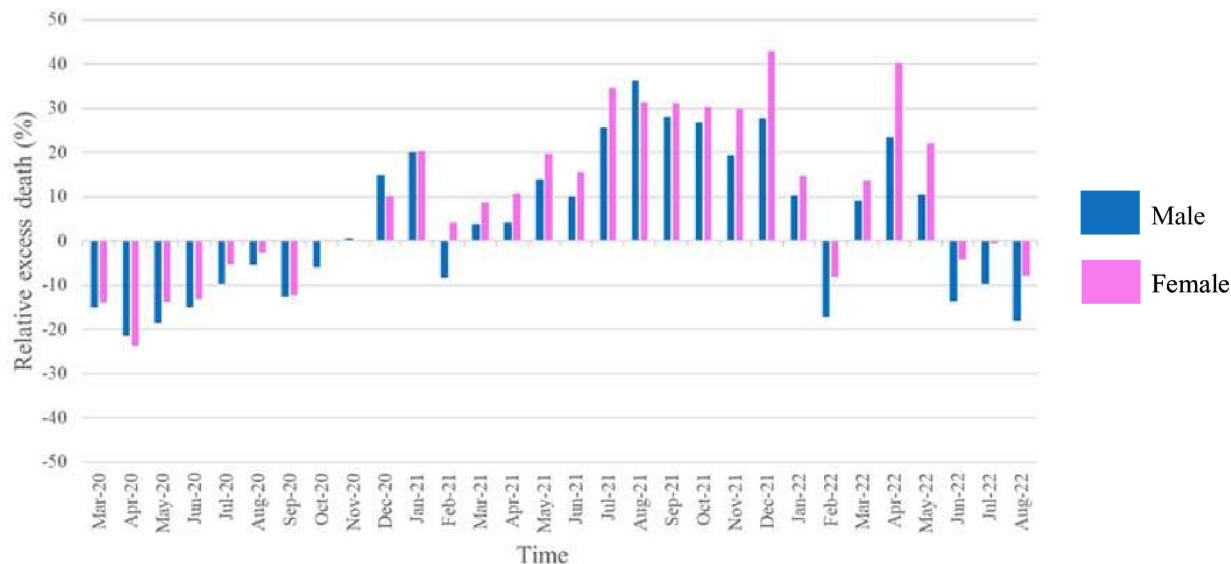


Figure 2 The relative excess mortality of end-stage renal disease patients by sex between March 2020 and August 2022

respectively. In 2020, there were erratic patterns of negative relative excess death in males and females. However, after January 2021, a clear pattern emerged showing the relative excess deaths in female patients were higher than that of male patients in all months, except August 2021. The gap between sex varied considerably by month in 2021 and 2022, ranging from a difference of almost zero in January 2021 to a 20-fold difference in July 2022. The relative excess deaths for males and females generally followed the same direction (either positive or negative values) in most months, except for November 2020 (male 0.5%, female -0.2%) and February 2021 (male -8.4%, female 4.2%).

More details on monthly excess deaths, excess deaths per 100 000 patients and relative excess death as per cent of expected deaths disaggregated by sex and age group are available in online supplemental tables 2 and 3a–3c.

DISCUSSION

This study finds a total of 4966 excess deaths during the 30-month observation period. We observed negative excess death among ESRD patients at the beginning of the pandemic in 2020, followed by a significant surge in excess deaths during waves 2–4. We hypothesise that the negative excess deaths in wave 1 were a result of the country's stringent lockdown measures, detection and isolation of confirmed cases and closure of international borders.⁴ This might result in very few overall COVID-19 cases, with only two COVID-19 deaths reported among the approximately 141 000 ESRD patients in 2020. Excess mortality increased in wave 2, reaching peak levels in wave 3 when the Delta strain was more transmissible and the surge cases overwhelmed healthcare facilities, disrupting the provision of essential health services for patients with chronic diseases, including ESRD patients who required three HD sessions per week. Additionally, Thailand's COVID-19 vaccine rollout in May 2021 faced significant

supply limitations until the end of the year.²³ This might have hampered access to vaccines for ESRD patients and contributed to the highest number of excess mortalities between July and December 2021 (679–979 deaths per month). In wave 4, the number of observed deaths began to taper off resulting in low to negative excess deaths. This was likely due to the less severe Omicron variant, increased vaccine coverage, health services resuming normal function and more relaxed travel restrictions. It should be noted that a downward trend line of expected deaths during the pandemic period was not because of a lower mortality rate but rather a reduction in newly diagnosed ESRD patients, likely stemming from service disruptions and travel restrictions.

In this study, the total number of all-cause excess deaths was much higher than the deaths from laboratory-confirmed COVID-19 cases in ESRD patients as reported by the civil registry. We speculate that several factors beyond COVID-19 infection might contribute to the observed all-cause excess mortalities, including overwhelmed healthcare services which disrupted HD and PD, patients' self-imposed restrictions on travelling to dialysis centres due to the fear of contracting COVID-19 infection, individual's intention to not put additional burden on health workers at the peak of managing COVID-19 patients, reduced public transport facilities, and stay-at-home policies. These circumstances might collectively lead to reduced access to essential services required by ESRD patients. Additionally, the under-reporting of COVID-19 confirmed deaths in the death registry could be another reason. It is unknown whether social stigmatisation hampered the reporting of COVID-19 deaths that occurred outside of hospitals, as observed in other studies.^{24 25}

Compared with the general population in Thailand, excess deaths per 100 000 population for ESRD patients are much higher. The estimated all-cause excess deaths

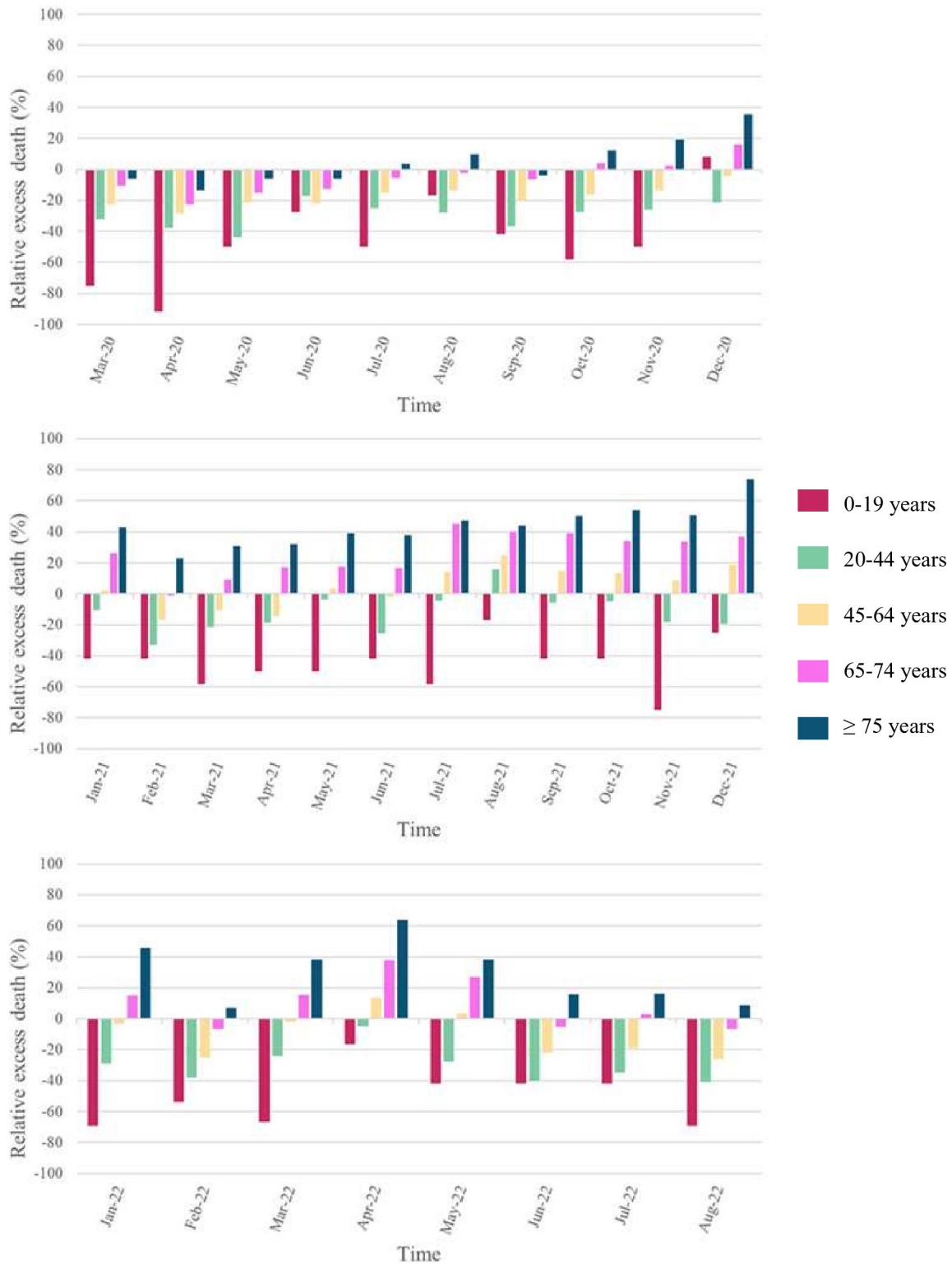


Figure 3 The relative excess death of end-stage renal disease patients by age group between March 2020 and August 2022

for the general population in Thailand between 1 January 2020 and 31 December 2021 was 35 200 (95% CI 26 600, 42 200), equal to 24.9 deaths (95% CI 18.7, 29.8) per 100 000 Thai population between 2020 and 2021.¹⁶ This is equivalent to one excess death per 100 000 Thai population per month. Our study found an average of 120 excess deaths per 100 000 ESRD patients per month (3600 per

100 000 patients in 30 months), indicating ESRD excess deaths as 120-fold (120/1) higher than the general population, notwithstanding the different study timeframe. Previous evidence also supported that COVID-19 affected ESRD patients more than the general population.¹⁴ The result of another study on excess death in the general Thai population between April and October 2021 was

25 486 (95% CI 13 913, 36 862), the relative excess death was 14.3% of expected deaths (95% CI 8.6%, 18.8%).²⁶ Compared with our estimates for ESRD patients during the same period (data not presented here), the relative excess death of ESRD patients in our study was approximately 1.6 (22.9/14.3) times that of the general Thai population.

There is no existing study estimating excess deaths among ESRD patients in Thailand. A study in the USA estimated 6953–10 316 excess deaths among 798 611 ESRD patients during February–August 2020, equivalent to 870.6–1291.7 per 100 000 ESRD patients.¹⁸ Our results on excess deaths in the same period were lower.

Our findings, which indicate that excess deaths were concentrated among older age groups and female ESRD patients, align with other studies presenting a correlation between older age and increased mortality in ESRD patients,^{27 28} and female CKD patients experiencing more excess deaths than males.²⁹ Higher excess deaths among older ESRD patients is also consistent with the pattern found in the general population which reported that people older than 60 years accounted for 78.4% of total excess deaths. However, the same study reported that males accounted for 56% of total excess deaths (14 223/25 486),²⁶ which is in contrast to our study in ESRD patients where males comprised only 26% of the total excess deaths (1284/4966). Pre-COVID-19 statistics of ESRD patients in Thailand also supported that more females than males experienced mortality in this population. Age structure by sex may help explain this finding as females in our cohort were older than males.

Several policies were introduced during the pandemic, such as mobilising surge capacity from within and outside health systems to contain the spread of infection, prevent health systems from getting overwhelmed, and sustain the provision of essential services, especially dialysis—a life-saving service for ESRD patients. ESRD was one out of seven chronic conditions prioritised for COVID-19 vaccination.

Our findings on excess deaths may be similar to what would be observed among other chronic disease patients who need essential healthcare services and close monitoring by healthcare practitioners during public health emergencies. Further research may explore excess mortality between PD and HD patients, and the status of COVID-19 vaccination. A regression analysis exploring factors affecting mortality among ESRD patients can shed light on mortality risk factors and further inform policies to reduce deaths.

Strengths and weaknesses of this study

The key strength of our study is the use of a national-level claims database which ensures completeness of the UCS population and their mortality outcome, thus minimising the risks of sampling bias. Additionally, the high coverage of death registration in Thailand (99.3% of total deaths), ensures confidence in the accuracy of the mortality outcome.

We identified certain limitations. First, we estimated monthly newly diagnosed ESRD patients by relying on historical service utilisation profile from 2015 until the previous month, which might not be completely accurate. Second, we expect that some ESRD patients may be underdiagnosed, especially during the second and third waves of the pandemic, which almost overwhelmed health delivery systems. This was reflected by the reduced number of patients diagnosed with ESRD in 2021–2022 compared with 2020, which can be explained by RRT service disruption. Third, confirmed COVID-19 deaths are likely under-reported, especially in 2020 due to overwhelmed COVID-19 testing capacities using RT-PCR, cases where COVID-19 patients passed away without a formal diagnosis, or discrepancies in clinicians certifying the cause of death when COVID-19 patients had multiple underlying diseases. Fourth, the data quality of all variables used in the regression model can affect the precision of estimating excess mortality and the robustness of the predictive model. Though we applied WHO's standard method of cyclic cubic regression spline models as the basis for modelling the expected deaths, the cubic splines interpolation algorithm does not work well for interpolation of highly fluctuated data and when there is a large time difference between the period fed into the predictive model and the estimated period.

CONCLUSION

We demonstrate the impact of the COVID-19 pandemic on all-cause excess mortality in ESRD patients. Older patients had higher all-cause excess mortality than the younger age groups. The SARS-CoV-2 virus strains with different infectivity and severity in different waves, and the health systems capacity to contain the pandemic and sustain the provision of essential health services to general patients including ESRD patients may have influenced variations in excess all-cause mortality. The all-cause mortality among ESRD patients in this study is far greater than that in the general population. Policies to minimise excess deaths should focus on sustaining provisions of essential services and rapid rollout of vaccination, especially in the older age group. We suggest further studies to investigate excess mortality between PD and HD patients, and the status of COVID-19 vaccination.

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Patient consent for publication Not applicable.

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Data availability statement Data may be obtained from a third party and are not publicly available. We only received permission to use this dataset for specific research objectives. We are not allowed to distribute patient dataset outside of the research team or use it for other purposes beyond the original agreed objectives. Researchers who are interested in using NHSO dataset can request access directly from the NHSO.

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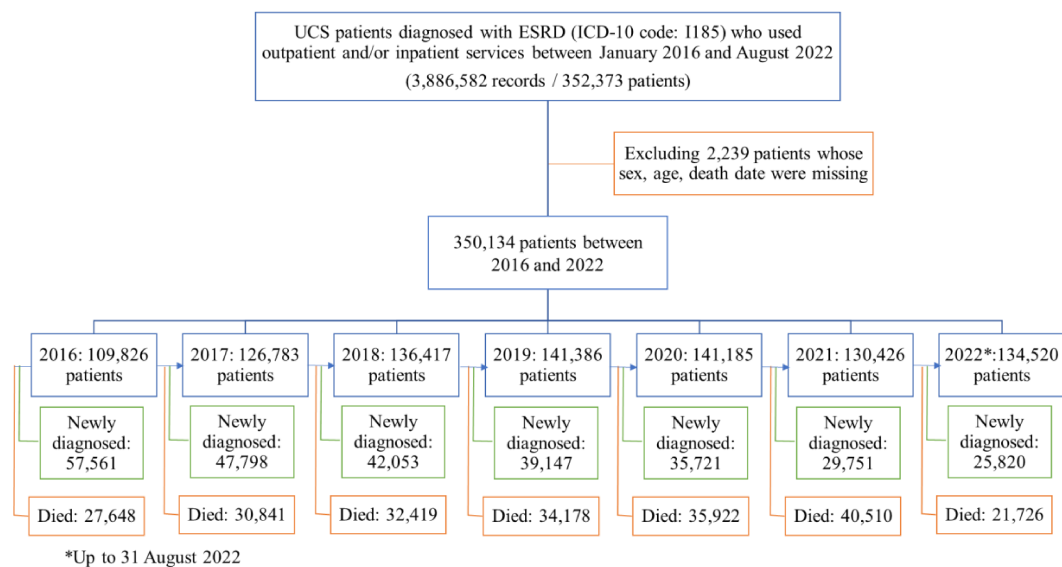
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Supplementary file

Figure 1 Population selection flow chart



Box 1 General additive models (GAM)

We used general additive models (GAM) to estimate expected number of deaths based on a negative binomial distribution to account for overdispersion and used the restricted maximum likelihood (REML) method to estimate the smoothing parameters of the model. The equation is:

$$Death_t = \beta_0 + \beta_1 * age_group_t + \beta_2 * sex_t + \log(population_t) + time_t$$

Where t is a given time point in the study period

$Death$ is an expected number of deaths in each time point t

age_group , sex is the factor variable directing a specific number of ESRD populations for each age group and sex in each time point t

We add the logarithm of the number of populations as an offset term and the time variable (integer represents time point t) as the smooth function of time accounting for seasonal fluctuation with a penalized cyclic cubic regression spline for our model.

Our model had an adjusted R^2 of 0.98. The result of the model fitting is shown in the table below

Variable	Coefficient	95% CI
Intercept	-4.68	(-4.79, -4.58)
age group 0-19	ref	-
age group 20-44	0.34	(0.23, 0.44)
age group 45-64	0.73	(0.62, 0.83)
age group 65-74	0.90	(0.8, 1.01)
age group ≥ 75	1.14	(1.04, 1.25)
Sex male	ref	-
Sex female	-0.07	(-0.09, -0.06)

The smooth term *time* had a p-value of less than 0.001 with a k-index 0.96, k^{\wedge} 28.0 and edf equal to 15.6.

Table 1. Positive excess mortality among ESRD patients between March 2020 and August 2022 by age group and sex.

a) Positive excess mortality by age group

Age group	Positive excess death (n)	Proportion
0-19	1	0.00
20-44	30	0.00
45-64	1,188	0.11
65-74	3,343	0.30
75 or more	6,525	0.59
Total	11,087	1.00

b) Positive excess mortality by sex

Age group	Positive excess death (n)	Proportion
Male	3,719	0.40
Female	5,490	0.60
Total	9,209	1.00

Table 2. Monthly excess all-cause mortality among ESRD patients between March 2020 and August 2022 disaggregated by sex

Month	Male				Female			
	Excess deaths (n)	Excess deaths per 100,000 (n)	Relative excess death		Excess deaths (n)	Excess deaths per 100,000 (n)	Relative excess death	
			%	95% CI			%	95% CI
Mar-2020	-238	-371.0	-15.0	-18.7, -11.3	-260	-337.0	-14.0	-17.7, -10.3
Apr-2020	-338	-527.3	-21.5	-25.5, -17.5	-437	-568.1	-23.8	-27.8, -19.8
May-2020	-283	-441.1	-18.6	-22.5, -14.4	-245	-319.2	-13.8	-17.8, -9.8
Jun-2020	-220	-342.0	-15	-18.9, -10.9	-224	-291.6	-13.1	-17.1, -9.3
Jul-2020	-140	-217.1	-9.7	-13.8, -5.6	-88	-114.8	-5.3	-9.4, -1.3
Aug-2020	-79	-122.4	-5.4	-9.3, -1.4	-46	-60.0	-2.7	-6.6, 1.1
Sep-2020	-187	-289.2	-12.6	-16.8, -8.6	-209	-272.6	-12.2	-16.1, -8.1
Oct-2020	-88	-135.5	-5.9	-9.9, -1.9	-3	-3.9	-0.2	-4.2, 3.8
Nov-2020	7	10.8	0.5	-3.4, 4.4	-4	-5.2	-0.2	-4.1, 3.6
Dec-2020	219	338.1	14.9	11, 19.1	169	221.2	10.1	6.1, 14
Jan-2021	288	445.0	20.0	16.1, 23.9	333	437.8	20.3	16.4, 24.1
Feb-2021	-118	-182.2	-8.4	-12.6, -4.4	67	88.3	4.2	0.3, 8.2
Mar-2021	51	78.6	3.8	-0.2, 7.7	129	170.2	8.5	4.5, 12.3
Apr-2021	51	79.0	4.1	0, 7.9	154	204.6	10.6	6.6, 14.4
May-2021	176	273.8	13.9	9.9, 17.9	282	377.1	19.7	15.7, 23.8
Jun-2021	126	196.6	9.9	5.9, 13.8	225	302.8	15.6	11.9, 19.6
Jul-2021	335	526.7	25.7	21.7, 29.8	505	687.9	34.6	30.7, 38.7
Aug-2021	478	758.8	36.3	32.4, 40.2	462	636.3	31.4	27.5, 35.2
Sep-2021	370	591.8	28.0	24.2, 32.1	459	638.4	31.2	27.2, 35.1
Oct-2021	351	565.9	26.8	22.9, 30.8	442	620.7	30.3	26.3, 34.3
Nov-2021	251	407.4	19.3	15.3, 22.9	431	611.9	29.8	25.9, 33.5
Dec-2021	361	592.0	27.7	23.7, 31.7	618	889.9	42.9	38.9, 46.8
Jan-2022	136	222.1	10.3	6.5, 14.1	213	306.1	14.7	10.8, 18.4
Feb-2022	-226	-366.4	-17.3	-21.2, -13.3	-118	-168.8	-8.2	-12.3, -4.5
Mar-2022	114	183.7	9.1	5.2, 13.1	189	269.2	13.7	9.8, 17.7
Apr-2022	282	454.0	23.5	19.4, 27.4	527	753.0	40.2	36.4, 44.1
May-2022	123	197.1	10.4	6.5, 14.6	285	405.5	22.1	18.2, 26.2
Jun-2022	-165	-262.3	-13.7	-17.7, -9.9	-57	-80.6	-4.3	-8.2, -0.5
Jul-2022	-121	-191.3	-9.7	-13.7, -5.7	-7	-9.9	-0.5	-4.6, 3.3
Aug-2022	-232	-365.5	-18.1	-22, -14.2	-110	-154.8	-7.9	-11.9, -4.1
Mar 2020 to Aug 2022	1,284	2,012.1	3.1	-0.8, 7.4	3,682	4,969.2	8.0	3.9, 12.4

Table 3. Monthly excess all-cause mortality among ESRD patients between March 2020 and August 2022 disaggregated by age group

a) Age 0-19 years and 20-44 years

Month	Age 0-19 years				Age 20-44 years			
	Excess deaths (n)	Excess deaths per 100,000 (n)	Relative excess death		Excess deaths (n)	Excess deaths per 100,000 (n)	Relative excess death	
			%	95% CI			%	95% CI
Mar-2020	-9	-809.4	-75.0	-83.3, -58.3	-61	-464.4	-32.1	-36.8, -27.9
Apr-2020	-11	-983.9	-91.7	-100.0, -75.0	-72	-544.3	-37.9	-42.6, -33.7
May-2020	-6	-533.3	-50.0	-50.0, -33.3	-81	-607.2	-43.5	-48.4, -38.7
Jun-2020	-3	-263.6	-27.3	-36.4, -18.2	-31	-230.7	-17.1	-21.5, -12.2
Jul-2020	-5	-435.2	-50.0	-70.0, -50.0	-45	-331.4	-25.1	-30.2, -20.1
Aug-2020	-2	-171.5	-16.7	-16.7, 0.0	-51	-372.3	-28.0	-32.4, -23.6
Sep-2020	-5	-421.6	-41.7	-50.0, -25.0	-69	-498.1	-36.7	-41.5, -31.9
Oct-2020	-7	-585.3	-58.3	-66.7, -41.7	-53	-378.0	-27.6	-32.3, -22.9
Nov-2020	-6	-497.9	-50.0	-58.3, -33.3	-50	-352.6	-25.9	-30.1, -21.8
Dec-2020	1	82.4	8.3	0.0, 25.0	-41	-287.6	-21.4	-25.5, -16.7
Jan-2021	-5	-405.2	-41.7	-50.0, -25.0	-20	-139.0	-10.5	-15.3, -5.8
Feb-2021	-5	-401.9	-41.7	-50.0, -25.0	-61	-421.0	-32.8	-37.6, -28.0
Mar-2021	-7	-555.1	-58.3	-58.3, -41.7	-38	-260.0	-21.2	-26.3, -17.3
Apr-2021	-5	-392.2	-50.0	-70.0, -50.0	-32	-217.7	-18.4	-23.6, -14.4
May-2021	-5	-387.9	-50.0	-70.0, -50.0	-6	-40.7	-3.5	-8.1, 1.2
Jun-2021	-5	-384.3	-41.7	-41.7, -25.0	-45	-303.5	-25.4	-29.9, -20.9
Jul-2021	-7	-528.7	-58.3	-66.7, -41.7	-8	-53.6	-4.4	-8.7, 0.0
Aug-2021	-2	-150.4	-16.7	-25.0, 0.0	30	200.5	16.0	11.2, 19.8
Sep-2021	-5	-372.9	-41.7	-58.3, -25.0	-11	-73.2	-5.8	-9.9, -1.0
Oct-2021	-5	-371.2	-41.7	-58.3, -25.0	-9	-59.6	-4.7	-9.4, -0.5
Nov-2021	-9	-661.3	-75.0	-91.7, -75.0	-35	-230.4	-18.0	-22.2, -13.9
Dec-2021	-3	-220.3	-25.0	-41.7, -25.0	-38	-249.3	-19.3	-23.9, -14.7
Jan-2022	-9	-649.4	-69.2	-76.9, -61.5	-58	-376.7	-29.0	-33.5, -25.0
Feb-2022	-7	-498.2	-53.8	-61.5, -46.2	-76	-488.7	-38.2	-42.2, -33.7
Mar-2022	-8	-560.6	-66.7	-83.3, -66.7	-46	-293.2	-24.0	-28.1, -19.3
Apr-2022	-2	-139.2	-16.7	-25.0, 0.0	-9	-57.2	-4.9	-9.2, -0.5
May-2022	-5	-342.2	-41.7	-50.0, -25.0	-50	-314.5	-27.5	-31.9, -22.5
Jun-2022	-5	-340.1	-41.7	-58.3, -25.0	-75	-466.9	-40.3	-45.2, -36.0
Jul-2022	-5	-339.0	-41.7	-58.3, -41.7	-67	-414.9	-34.7	-39.4, -30.1
Aug-2022	-9	-605.7	-69.2	-84.6, -61.5	-81	-499.3	-40.9	-45.5, -36.4
Overall	-166	-12,779.1	-46.6	-51.7, -39.5	-1,289	-8,781.85	-22.9	-26.3, -19.3

b) Age 45-64 and 65-74 years

Month	Age 45-64 years				Age 65-74 years			
	Excess deaths (n)	Excess deaths per 100,000 (n)	Relative excess death		Excess deaths (n)	Excess deaths per 100,000 (n)	Relative excess death	
			%	95% CI			%	95% CI
Mar-2020	-262	-480.9	-22.5	-26.0, -18.8	-101	-263.0	-10.4	-14.0, -6.7
Apr-2020	-327	-600.0	-28.2	-32.2, -24.3	-218	-569.2	-22.6	-26.6, -18.7
May-2020	-241	-441.5	-21.4	-25.4, -17.4	-140	-366.3	-15.0	-18.9, -11.1
Jun-2020	-237	-431.9	-21.8	-25.6, -17.9	-112	-293.1	-12.5	-16.5, -8.6
Jul-2020	-163	-296.0	-15.2	-19.2, -11.2	-48	-125.8	-5.5	-9.4, -1.5
Aug-2020	-146	-264.0	-13.5	-17.3, -9.6	-20	-52.5	-2.3	-6.1, 1.6
Sep-2020	-227	-408.7	-20.5	-24.4, -16.5	-58	-152.7	-6.5	-10.5, -2.4
Oct-2020	-185	-331.1	-16.4	-20.4, -12.6	35	92.1	3.9	-0.1, 7.8
Nov-2020	-152	-271.1	-13.5	-17.3, -9.7	22	57.9	2.4	-1.4, 6.3
Dec-2020	-50	-89.0	-4.5	-8.4, -0.5	142	375.9	16.0	12.1, 20.1
Jan-2021	24	42.6	2.2	-1.5, 6.0	229	610.3	26.4	22.6, 30.3
Feb-2021	-178	-315.6	-16.7	-20.7, -12.8	-10	-26.7	-1.2	-5.2, 2.7
Mar-2021	-108	-190.6	-10.5	-14.5, -6.7	75	200.7	9.4	5.4, 13.1
Apr-2021	-143	-252.9	-14.4	-18.4, -10.6	132	356.5	17.2	13.3, 21.0
May-2021	32	56.8	3.3	-0.6, 7.3	132	359.0	17.5	13.6, 21.6
Jun-2021	-21	-37.3	-2.1	-5.9, 1.7	128	350.6	16.8	13.1, 20.7
Jul-2021	139	247.9	13.7	9.8, 17.8	347	966.1	45.1	41.2, 49.2
Aug-2021	255	458.2	24.8	21.0, 28.6	311	877.2	40.1	36.2, 43.8
Sep-2021	150	270.7	14.5	10.7, 18.4	303	866.4	39.1	35.4, 43.0
Oct-2021	137	248.5	13.2	9.5, 17.2	260	752.5	33.9	30.0, 37.8
Nov-2021	91	165.8	8.8	5.0, 12.6	255	748.0	33.6	29.6, 37.2
Dec-2021	196	359.7	18.9	14.9, 22.7	279	830.6	36.8	32.8, 40.8
Jan-2022	-36	-65.8	-3.4	-7.2, 0.3	115	341.6	15.0	11.2, 18.7
Feb-2022	-262	-475.7	-25.2	-29.2, -21.4	-51	-150.6	-6.7	-10.6, -2.9
Mar-2022	-21	-37.9	-2.1	-5.9, 1.8	111	325.7	15.2	11.4, 19.2
Apr-2022	133	240.2	13.9	10.0, 17.7	263	773.4	37.8	34.0, 41.6
May-2022	31	55.7	3.3	-0.6, 7.2	184	540.1	27.0	23.2, 30.9
Jun-2022	-209	-373.0	-21.8	-25.7, -18.1	-37	-107.8	-5.3	-9.2, -1.6
Jul-2022	-188	-334.0	-19.0	-22.9, -15.1	20	58.1	2.8	-1.1, 6.8
Aug-2022	-264	-467.1	-25.9	-29.7, -22.2	-49	-141.9	-6.6	-10.4, -2.7
Overall	-2,232	-4,021.9	-7.1	-10.6, -3.4	2,499	6,853.4	10.3	6.2, 14.7

c) Age 75 years or more

Month	Age 75 years or more			
	Excess deaths (n)	Excess deaths per 100,000 (n)	Relative excess death	
			%	95% CI
Mar-2020	-65	-190.2	-5.9	-9.6, -2.4
Apr-2020	-147	-433.8	-13.6	-17.5, -9.7
May-2020	-60	-178.3	-5.8	-9.7, -1.7
Jun-2020	-61	-182.1	-6.1	-9.9, -2.2
Jul-2020	33	99.4	3.4	-0.5, 7.4
Aug-2020	94	285.3	9.7	5.9, 13.5
Sep-2020	-37	-112.9	-3.8	-7.7, 0.1
Oct-2020	119	365.7	12.1	8.2, 15.9
Nov-2020	189	586.5	19.4	15.5, 23.2
Dec-2020	336	1,057.7	35.5	31.6, 39.4
Jan-2021	393	1,253.2	42.8	39.0, 46.5
Feb-2021	203	654.4	23.0	19.1, 27
Mar-2021	258	838.9	30.8	27.0, 34.6
Apr-2021	254	838.4	31.9	28.1, 35.8
May-2021	305	1,020.2	39.2	35.2, 43.1
Jun-2021	294	999.6	37.8	34.1, 41.6
Jul-2021	369	1,282.1	47.2	43.2, 51.2
Aug-2021	346	1,226.5	44.1	40.3, 48
Sep-2021	392	1,416.5	50.4	46.5, 54.2
Oct-2021	410	1,513.2	53.8	49.9, 57.6
Nov-2021	380	1,433.3	50.7	46.8, 54.3
Dec-2021	545	2,116.7	73.8	70.1, 77.8
Jan-2022	337	1,313.9	45.6	41.8, 49.3
Feb-2022	52	202.4	7.1	3.2, 10.9
Mar-2022	267	1,037.7	38.3	34.4, 42.1
Apr-2022	424	1,659.1	64.0	60.2, 67.7
May-2022	248	967.8	38.1	34.3, 42.1
Jun-2022	104	404.1	15.7	12.1, 19.6
Jul-2022	112	434.2	16.4	12.4, 20.2
Aug-2022	61	236.7	8.7	4.9, 12.6
Overall	6,155	20,534.8	24.5	19.8, 29.4

